Bone Loss in Adolescents After Bariatric Surgery

WHAT'S KNOWN ON THIS SUBJECT: The rate of bariatric surgery in teenagers is increasing rapidly, but little is known about its effects on bone health in such a young population.

WHAT THIS STUDY ADDS: Adolescents will lose some bone density in the first 2 years after bariatric surgery, but the *z* score does not typically fall below average for age and gender.

abstract

OBJECTIVE: To evaluate bone loss in adolescents after Roux-en-Y gastric bypass surgery and to determine the extent to which bone loss was related to weight loss. We hypothesized that adolescents would lose bone mass after surgery and that it would be associated with weight loss.

PATIENTS AND METHODS: We conducted a retrospective case review of 61 adolescents after bariatric surgery. Whole-body bone mineral content (BMC) and density (BMD) were measured by dual-energy radiograph absorptiometry, and age- and gender-specific BMD *z* scores were calculated. Measurements were obtained when possible before surgery and then every 3 to months after surgery for up to 2 years. Data were analyzed by using a mixed-models approach, and regression models were adjusted for age, gender, and height.

RESULTS: Whole-body BMC, BMD *z* score, and weight decreased significantly over time after surgery ($P < .0001$ for all). In the first 2 years after surgery, predicted values on the basis of regression modeling for BMC decreased by 7.4%, and BMD *z* score decreased from 1.5 to 0.1. During the first 12 months after surgery, change in weight was correlated with change in BMC ($r = 0.31$; $P = .02$). Weight loss accounted for 14% of the decrease in BMC in the first year after surgery.

CONCLUSION: Bariatric surgery is associated with significant bone loss in adolescents. Although the predicted bone density was appropriate for age 2 years after surgery, longer follow-up is warranted to determine whether bone mass continues to change or stabilizes. *Pediatrics* 2011;127:e956–e961

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KEY WORDS

bone density, bariatric surgery, obesity, weight loss, adolescents

ABBREVIATIONS

RYGB—Roux-en Y gastric bypass
WB—whole body
BMC—bone mineral content
BMD—bone mineral density
DXA—dual-energy radiograph absorptiometry

www.pediatrics.org/cgi/doi/10.1542/peds.2010-0785

doi:10.1542/peds.2010-0785

Accepted for publication Dec 17, 2010

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

Funded by the National Institutes of Health (NIH).

The number of obese adolescents in the United States has risen during the past decade.[1] Currently, 18.1% are obese (BMI ≥ 95th percentile for age).[2] Extremely obese adolescents (BMI > 99th percentile, estimated at 2%–6%)[3] are of particular concern because they are at an increased risk of premature morbidity and mortality.[4–6] Unfortunately, treatment with behavior modification or medication has not resulted in significant long-term improvements.[7] As a consequence, increasing numbers of adolescents are electing to have bariatric surgery, commonly the Roux-en Y gastric bypass (RYGB) procedure, to treat obesity. From 2000 to 2003, the number of patients younger than 20 who had bariatric surgery in the United States increased threefold, from 222 to 771.[8]

Adolescents who undergo RYGB experience dramatic weight loss, losing 58% to 73% of their excess weight by 1 year.[9–12] However, the long-term consequences of this surgery at such a young age are still not well understood. Adult studies have demonstrated a decrease in bone mass and density after RYGB surgery,[13–20] with the extent of bone loss related to the amount of weight loss.[17,18] However, no studies have looked at the bone mass changes after RYGB in adolescents. Loss of bone mineral at the age when they should be approaching peak bone mass (estimated at age 20)[21] could potentially compromise their future bone health. The objectives of this study were to evaluate changes in bone mass and density in adolescents after bariatric surgery, and to determine if bone changes were related to weight loss. Our hypotheses were that adolescents would experience a decrease in whole-body (WB) bone mineral content (BMC) and bone mineral density (BMD) *z* scores after surgery, and this loss would be related to the amount of weight lost.

PATIENTS AND METHODS

A retrospective chart review was performed for 102 adolescents who underwent laparoscopic RYGB surgery at Cincinnati Children's Hospital from 2001 to 2008. The chart review was approved by our institutional review board before beginning the study. All individuals who underwent surgery fulfilled the following criteria[22]: (1) failed >6 months of organized weight loss attempts; (2) had a BMI > 35; (3) had 1 or more obesity-related comorbid conditions; (4) completed most of their linear growth (male patients, Tanner stage 4; female patients, postmenarche); and (5) passed a psychological evaluation. The psychological evaluation was performed to make sure that the patient had the intellectual capacity to understand the necessary lifestyle changes as well as the risks and adverse effects of the surgery, and that the patient had enough family support to follow the postoperative plan of care. Comorbidities such as depression were considered from the standpoint of ensuring that they were adequately being managed before introducing the complexity of an invasive obesity treatment intervention.[22] There are no specific age limits for being considered for weight loss surgery at our institution. Each surgery was performed by 2 pediatric surgeons. The procedure resulted in a gastric pouch of ~30 to 45 mL and a Roux limb of 75 to 150 cm. After the surgery, patients were instructed to take a multivitamin that contained 1000 mg calcium and 800 IU of vitamin D daily.

Because bariatric surgery was new to our institution, and a cautious approach seemed prudent, patients had dual-energy radiograph absorptiometry (DXA) scans before surgery, and then every 3 to 6 months after surgery for 2 years. DXA scans were originally performed to document changes in lean mass for clinical purposes. Currently, DXA scans are being performed less frequently. Scans were acquired on 2 different machines; both were the same model (Hologic 4500A [Hologic, Inc, Bedford, MA) and were cross-calibrated. Patients were scanned on the same machine throughout. Because of the technical limitations of the densitometers, only patients who weighed <136 kg before 2005 or <159 kg after 2005 (updated model) could be scanned. Therefore, for some patients, the first DXA could not be obtained until they had lost enough weight postoperatively. All DXA scans were analyzed by using software version 12.4 for calculation of WB BMC and BMD. *z* scores that reflected BMD for chronological age were generated from the Hologic software. Because *z* scores for male patients older than 20 cannot be calculated from these reference data, we calculated *z* scores for the 2 male patients older than 20 (20.2 and 20.4 years at baseline) as if they were 20 years of age.

We chose to evaluate both WB BMC as well as BMD *z* score because they provide related but slightly different information. BMC is a measure of the absolute amount of bone mineral (g). BMD (g/cm^2) is BMC divided by the bone area (cm^2) to adjust for bone size. The BMD *z* score reflects the bone density relative to age- and gender-specific norms. We reported both the BMC and BMD *z* scores in this study so we could accurately portray both the true total change in bone, and how it compares to other adolescents of similar age. Also, we used the WB, not WB less head measurements because head makes up a constant amount of the WB BMC in this age group. Inclusion of the head should not have affected the results because it is a constant across all patients.

Data on presurgery height, weight, chronic illness, medication use, reproductive history, and demographics

were abstracted from medical charts. Height and weight were measured by the clinic staff. Height was measured using a calibrated wall-mounted stadiometer (Aryton Stadiometer Model S100 [Aryton, Prior Lake, MN]). Weight was measured using a digital scale (Model 5002 Stand-On Scale [Scale Tronix, White Plains, NY]), with patients dressed in lightweight clothing, without shoes. BMI was calculated as weight divided by height squared (kg/m^2). *z* scores for height were calculated relative to the Centers for Disease Control and Prevention 2000 growth charts using Epi Info 3.5.1 (Centers for Disease Control and Prevention, Atlanta, GA). BMI *z* scores at this extreme of obesity are not valid.[3]

Of the original 102 patients, 61 were included in the analyses. Reasons for exclusion of 41 patients were as follows: 17 never had a DXA scan; 8 had only 1 scan; the first DXA scan for 8 patients was >6 months after the surgery; and 8 were excluded for medical conditions that can affect bone density (high-dose oral steroids during the follow-up period [$n = 4$], wheelchair-bound because of spina bifida [$n = 1$], Depo-Provera use [$n = 2$], and pregnancy before surgery [$n = 1$]). Three patients had pregnancies after surgery; DXA scans acquired after pregnancy were excluded.

Statistical analyses were conducted by using SAS 9.1 (SAS Institute, Inc, Cary, NC). The primary statistical method used was mixed modeling, which accounts for multiple measurements per individual obtained at different time points. All analyses were conducted using a random coefficient model with the intercept being random and a covariance structure of variance components. The first set of analyses investigated trends in BMC, BMD *z* score, and weight loss over time since surgery. Polynomial terms were fitted, and the residuals were evaluated to determine the best fit of the models. For those individuals whose first scan was before surgery, we recoded time since surgery as 0. In all analyses, the potential covariates examined were height, age at surgery, and gender. Race was not included as a covariate because we only had 6 nonwhite patients. Exclusion of nonwhite patients did not change the findings. The covariate variables were entered and removed by backward elimination; variables were kept if their *P* value was ≤.05. Because of the small sample size, we did not examine interactions among all covariates. Because only half of the patients had a scan in the second year, we repeated the analyses in the subset of patients ($N = 34$) who had at least 1 additional DXA scan between 12 and 24 months after surgery to confirm patterns of change over time.

The second set of analyses investigated the extent to which weight loss could account for bone loss after surgery. Because of the curvilinear nature of weight loss over time, these analyses were restricted to data obtained in the first year after surgery ($N = 52$). Nine patients were excluded because the second DXA scan was not performed until after 12.0 months. First, we examined the correlation between change in weight and change in bone measures. Change variables were calculated as the difference between the last minus the first measurement within that time interval. Next, we fitted weight along with time since surgery in the models to predict BMD *z* score and BMC, and we evaluated the change in the regression coefficient for time with and without weight in the model.

TABLE 1 Descriptive Characteristics of Study Participants at the Time of Surgery

	Female Participants	Male Participants	Total
n (%)	51 (84)	10 (16)	—
Race, *n* (white/black)	48:3	7:3	90% white
Age, mean ± SD (range), y	17.3 ± 2.0 (13.7–23.5)	17.3 ± 1.9 (14.5–20.2)	17.3 ± 1.9
BMI, mean ± SD (range)	54.3 ± 7.0 (41.4–66.6)	55.1 ± 6.0 (44.4–64.5)	54.4 ± 6.8
Weight, mean ± SD (range), kg	152.4 ± 21.0 (111.3–203.2)	167.0 ± 11.6 (141.5–181.5)	154.8 ± 20.4
Height, mean ± SD (range), cm	167.5 ± 6.9 (154.6–182.5)	174.3 ± 7.3 (158.0–181.6)	168.7 ± 7.4
Height *z* score, mean ± SD (range)	0.7 ± 1.1 (−1.3–3.2)	0.0 ± 0.8 (−1.3–1.5)	0.6 ± 1.1

RESULTS

Descriptive characteristics of the 61 patients are shown in Table 1. Preoperatively, 18% had nonalcoholic fatty liver disease, 30% had hypertension, 33% had depression, 63% had sleep apnea, 11% had type 2 diabetes mellitus, and 28% of the female patients had polycystic ovary syndrome. Linear growth was minimal in our patients. The mean ± SD change in height was 0.2 ± 0.8 cm (range −2.7 to 2.5 cm). No patients needed treatment for bone-related problems during the study period.

Patients had an average of 3 DXA scans (range: 2–6). The first DXA scan was obtained at the following times: before surgery ($n = 22$); within 3 months after surgery ($n = 19$); and between 3 and 6 months after surgery ($n = 20$). The time of the last scan varied (mean: 13.9 months [range: 2.8–26.8]).

Weight, WB BMC, and BMD *z* score decreased significantly over time after surgery ($P < .0001$ for all) (Fig 1). Regression models were for weight (Fig 1A), gender, time, and time^2; for BMC (Fig 1B), height, gender, time, and time^2; and for *z* score (Fig 1C), age and time. Weight was not included in the models for BMC and *z* score so that we could evaluate the change in these variables over time separate from change in weight.

Weight showed a pronounced curvilinear decline over time (time squared

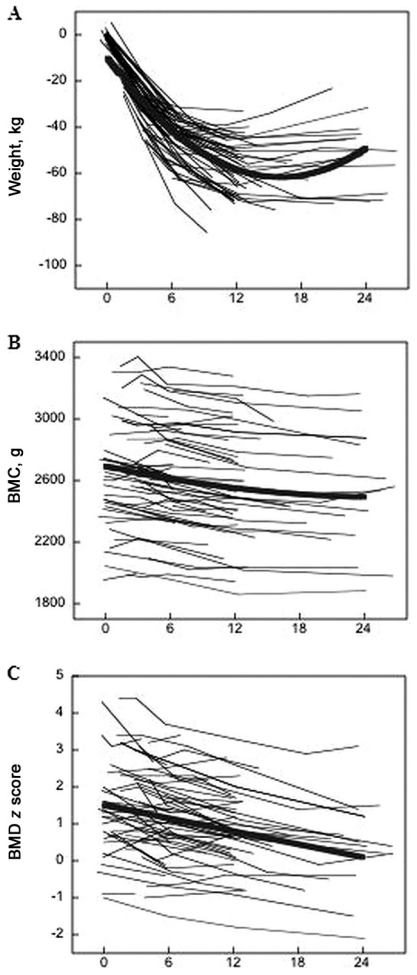

FIGURE 1
Weight (A), BMC (B), and BMD *z* score (C) over time after bariatric surgery. Lines represent the 61 patients. The bold line is the predicted value for the regression characterizing change over time.

term, $P < .0001$) (Fig 1A). Weight loss was greatest in the first year and then stabilized. Some patients had slight increases in weight after 15 months. On the basis of the regression model, the predicted weight loss at 6, 12, 18, and 24 months after surgery was 41.4 ± 1.3, 58.4 ± 1.4, 61 ± 1.5, and 49.2 ± 2.1 kg, respectively. Gender was a significant covariate in the regression model with male patients losing more weight (6.4 kg) than female patients.

BMC showed a slight curvilinear decline over time (time-squared term, $P < .0001$) (Fig 1B). Predicted values on the basis of regression modeling for WB BMC were 2692 g before surgery, decreasing to 2552 g at 1 year after surgery (−5.2%) and 2494 g at 2 years after surgery (−7.4%). Height and gender were significant covariates in the regression model. Height was positively associated with BMC (18.95 g/cm; $P < .0001$), and male patients had more BMC than female patients (323.4 g; $P = .0004$). For the patients who may still be growing, including height in the regression models accounted for the differences in bone mass and density because of linear growth.

BMD *z* score decreased linearly over time ($P < .0001$) (Fig 1C). The predicted values for BMD *z* score on the basis of regression modeling were 1.5 before surgery, decreasing to 0.8 at 1 year after surgery and 0.1 at 2 years after surgery. Although the *z* score decreased over time, the *z* score remained above average for age throughout the 2-year follow-up period. Age was included in the regression model because it was negatively associated with BMD *z* score (−0.056 per year; $P = .03$).

Results of the regression models for weight, WB BMC, and BMD *z* score were similar when restricting the analyses to the subset of individuals ($N = 34$) that had at least 1 additional measurement >12 months after surgery.

We examined the potential effect of weight loss for mediating or "explaining" the skeletal changes after surgery. Because of the pronounced curvilinear trend in weight loss over time, we restricted this set of analyses to those measurements that occurred within the first 12 months after surgery. The correlation between change in weight and change in BMC was $r = 0.31$ ($P = .02$), and the correlation between change in weight and change in BMD *z* score was $r = 0.05$ ($P = .73$). The correlations with BMC and BMD *z* score were not different when expressing weight change in absolute terms or as a relative value (eg, percentage of total weight).

We then fitted weight in the regression models to predict BMD *z* score and BMC. When both weight and time after surgery were included in the regression model that predicted BMD *z* score, the regression coefficient for time after surgery was attenuated by 44% (−0.052 vs −0.029) and was no longer statistically significant ($P = .20$). Inclusion of weight in the model for BMC resulted in a 14% reduction in the regression coefficient for time (−11.15 vs 9.64); however, it remained statistically significant ($P = .01$).

DISCUSSION

In this study a decrease in WB BMC of 5.2% by 1 year and of 7.4% by 2 years after bariatric surgery in adolescents is demonstrated. The loss in WB BMC was significantly correlated with the change in weight, accounting for 14% of the decrease in BMC in the first year after surgery. Although BMD values declined significantly (from 1.5 to 0.1), the BMD *z* score did not fall below the expected value for gender and age (ie, a *z* score of 0) by 2 years after surgery. This finding is likely to be a consequence of the high bone mineral content and density before surgery in this extremely obese population. However, if bone loss continues, even at a slow rate, these patients may have an increase risk of fractures later in life.

Studies of adults also have reported bone loss after bariatric surgery.[13–20] Decreases in WB BMC were 3% to 12% at 9 to 24 months after surgery,[14,20] and adults had a fracture rate of 5% in the first 2.4 years after surgery.[23] In addition, the magnitude of bone lost in adults after RYGB procedures has been shown to be associated with the amount of weight lost.[15,17,18] Our study shows that weight loss was significantly associated with bone loss after

surgery but could only account for a small amount of the variability in bone loss (14% for BMC).

There are several potential mechanisms that may result in bone loss after bariatric surgery. First, weight loss by itself may result in loss of bone mass. In several studies of adults it is shown that nonsurgical weight loss is often accompanied by bone loss as measured by DXA.[24,25] Second, decreased food intake and alterations in absorption of nutrients such as calcium[26] may result in nutritional deficiencies that contribute to bone loss after bariatric surgery. The possibility for nutritional deficiencies among adolescents is especially concerning because of their potential lack of compliance with dietary recommendations and vitamin replacement after surgery[27,28] and the cumulative effect on nutritional status for many decades.

Third, other hormones have been implicated in causing bone loss after bariatric surgery. Insulin-like growth factor 1,[13] leptin,[14,29] and ghrelin[14] are decreased postoperatively. Adiponectin was found to be increased after surgery and correlated with bone loss in a study of adults.[18] Recent data revealed that gut-derived serotonin affects bone formation[30]; it is unknown whether bariatric surgery affects this hormone and whether it has a role in bone loss after RYGB surgery.

Our study has several limitations. First, although our original sample size was large, 32% of the patients had to be excluded because they exceeded the weight limit of the densitometer. This creates a selection bias because the patients at the extremes of morbid obesity could not be evaluated. Also, we did not get a baseline scan until after surgery on 64% of the patients, and there was a wide variability in the timing of the first DXA scan and in the number of follow-up scans. Second, we used WB DXA measurements, which may not be as good as regional scans for predicting fractures at specific skeletal sites. Third, changes in tissue thickness around bone that result from weight loss can result in higher WB BMC and BMD values as measured by the Hologic densitometer;[31] thus our findings may underestimate the true degree of bone loss.

Also, because this was a retrospective study in which clinic data were used, height and weight may not have been recorded as precisely as if multiple measurements had been obtained by highly trained research staff. However, there was little variability in height between visits, mitigating this concern. In addition, we were unable to accurately determine the compliance rate of the patients taking calcium and vitamin D supplements, and whether it had any effect on bone changes. Because of these limitations, additional studies should be performed to verify our findings.

Finally, we do not know the long-term effect of RYGB surgery on bone, because our study was limited to 2 years after surgery. Despite these limitations, our study extends the understanding of the consequences of bariatric surgery on bone health because it is the first longitudinal study in which bone mass in adolescents is examined and followed up to 2 years after surgery.

It is reassuring that these patients began with greater BMD *z* score than expected (ie, 1.5 SD higher), and BMD did not typically fall below average during the 2 years after surgery. However, the clinical consequences of losing bone mass after RYGB performed in the adolescent years are unknown. Therefore, these adolescents need to be followed long-term to determine if the decrease in BMD *z* score continues and increases their risk for future fractures. As bariatric surgery becomes more common in younger individuals, its effect on bone mass and the clinical consequences need to be better understood. This is especially important for primary care physicians, who will continue to provide routine medical care for these patients. The primary care physician should be aware of the possibility of low bone mass in adolescents after bariatric surgery so that bone mass can be monitored and managed appropriately.

CONCLUSIONS

In our study, a 7.4% decline in WB BMC over 2 years was shown in adolescents who underwent bariatric surgery. The decrease in bone mass was associated, to a small extent (14% for BMC), with weight loss in the first year. Future studies are needed to elucidate the types of weight loss (lean versus fat mass) and molecular pathways that influence changes in bone mass, and the clinical consequences of these changes.

ACKNOWLEDGMENTS

This is a hybrid article of the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) Consortium (National Institutes of Health grant U01 DK072493) (principal investigator is Dr Inge). Some patients in this study were enrolled in Teen-LABS.

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